II.

Election/Restriction

Applicants note that the restriction/electionrequirement has been made final, and claims 8 and 13-15 are being examined to the extend as they relate to NL1. (The reference to claims 1-7 on page 3, line 19 of the Office Action is believed to be in error.)

III.

Drawings

Applicants note the objections to the drawings, but intend to delay the filing of corrected drawings and of corresponding amendments to the specification until after allowable subject matter is indicated.

IV.

Specification

Applicants were requested to correct certain typographical errors in the specification, and to add ATCC deposit number and the new address of ATCC. The requested amendments have been instructed in the foregoing amendment to the specification, and are believed to overcome the objection on this ground.

V.

Claim Objections

Claims 8 and 13-15 were objected to a being drawn to non-elected inventions (NL5, NL8, or an antibody according to claim 9.) As the claims are not directed to NL1 and related subject matter, the withdrawal of this objection is respectfully requested.

VI.

Claim Rejections - 35 USC §112, first paragraph

Claims 8 and 13-15 were rejected under 35 U.S.C. §112, first paragraph, because the specification, in the Examiner's view, "does not reasonably provide enablement for a polypeptide which shares at least 90% identity with amino acids 270-493 (the fibrinogen domain) of SEQ ID NO: 2. The Examiner specifically noted that:

1. the claims contain "no structural limitation on the N-terminal half of the polypeptide", and "no functional limitation";

2. no "function has been assigned to the fibrinogen domain";

3. according to Davis et al. (7) little is known about the function of the fibrinogen-like and coiled-coil N-terminal regions within the hTL1 ligand sequence;

4. the specification does not disclose to which receptor NL1 binds;

5. there is no disclosure of the amino acids or regions required for receptor binding; and

6. one would not know how to use a modified fibrinogen-like domain or a polypeptide containing it.

Without acquiescence in the Examiner's position or in any part of the rejection, the claims now recite a polypeptide comprising the amino acid sequence of NL1 (claim 8), a polypeptide comprising amino acids 270-493 (the fibrinogen-like domain) of NL1 (claim 23), or conjugates of such polypeptides with immunogenic proteins (claims 24 and 25). It is submitted that the specification provides sufficient enablement for these polypeptides.

The Examiner specifically acknowledged that the specification is enabling for a polypeptide comprising the sequence of SEQ ID NO: 2; this embodiment is claimed in claim 8. The specification is also enabling for polypeptides comprising amino acids 270-493 of NL1 (claim 23). The fibrinogen-like region within the NL1 amino acid sequence is sufficiently long to serve as a target for the generation of NL1-specific antibodies, which, in turn, can be used (alone or as antibody mixtures), for example, to detect NL1 in a biological sample. Such antibodies can also be used for the purification of a native NL1 polypeptide. This is clearly taught, e.g. at pages 19-29, and 44-45 of the specification. It is noted that even if the antibodies generated to the fribrinogen-like region, or a longer (non-native) polypeptide comprising it, do not react or react poorly with a native NL1 polypeptide, they might specifically bind a reduced (linearized) form of the native molecule, and can, therefore, be used, for example, in expression experiments to determine the expression levels of the NL1 polypeptide. The conjugates claimed in claims 24 and 25 may be used for immunization of mammals, and are disclosed at pages 21-22.

In view of the foregoing amendments, the reconsideration and withdrawal of this rejection is respectfully requested.

VII.

Claim Rejections - 35 U.S.C §112, second paragraph

(a) Claim 1 and dependent claims 2-7 were rejected under 35 U.S.C. §112, second paragraph as "being indefinite" in their recitation of sequence "identity", as term, which - in the Examiner's view- is not properly defined in the specification.

Since claims 1 and 2-7 have been withdrawn from consideration, their rejection appears to be in error. The rejection, to the extent it was intended to concern elected claims 8, and 13-15 is believed to be moot, since these claims no longer contain the "sequence identity" language. It is emphasized, however, that the claims were amended without acquiescence in the Examiner's position. Applicants specifically retain the right to pursue claims using the "sequence identity" language in continuing or other related applications, taking issue with the Examiner's position concerning the definiteness of this language.

(b) Claim 8 rejected as "indefinite" for its use of a parenthetical term after the name of the ligand "NL1". In view of the current amendment of claim 8, this rejection is believed to be moot.

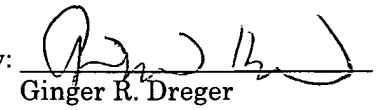
© Claim 14 was rejected as "indefinite" in its recitation of a "further" therapeutic or cytotoxic agent. As the term "further" has been deleted from claims 14 and 15, the withdrawal of this rejection would be in order.

(d) Claim 15 was rejected for its reference to the VEGF "family", which was thought to be indefinite. The claim now recites VEGF, which is clearly defined, e.g. at page 7, lines 11-25, therefore, the Examiner is respectfully requested to withdraw this rejection.

Applicants note that the claims were found to be free of prior art. As the present application is believed to be in *prima facie* condition for allowance, an early action to that effect is respectfully solicited.

Respectfully submitted,
GENENTECH, INC.

Date: October 6, 1998

By: 
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